```
     FILE 'REGISTRY' ENTERED AT 07:47:36 ON 24 JAN 2004
L1          2496 S VANAD? AND (CYCLOPENTADIEN? OR DICYCLOPENTADIEN? OR BISCYCLOP

     FILE 'CAPLUS' ENTERED AT 07:49:28 ON 24 JAN 2004
L2          1309 S L1
L3           811 S VANAD? (10A) (CYCLOPENTADIEN? OR DICYCLOPENTADIEN? OR BISCYCL
L4          1512 S L2 OR L3
L5          1551 S L4 OR VANADOCEN?
L6             1 S L5 (200A) (ANGIOGEN? OR ANTIANGIOGEN? OR (INHIBIT? (10A) (BLO
L7             0 S L5 (200A) (VASCULAR? OR DIABET?)

     FILE 'MEDLINE, WPIDS, CANCERLIT, DRUGU, IMSDRUGCONF, JAPIO, MEDICONF,
     PHARMAML, PHIC, PHIN' ENTERED AT 07:58:09 ON 24 JAN 2004
L8           109 S VANAD? (20A) (CYCLOPENTADIEN? OR DICYCLOPENTADIEN? OR BISCYCL
L9           189 S L8 OR VANADOCEN?
L10            1 S L9 (200A) (ANGIOGEN? OR ANTIANGIOGEN? OR (INHIBIT? (10A) (BL
L11            1 S L9 (200A) (VASCULAR? OR DIABET?)
L12            2 S L10 OR L11
L13            1 S L9 AND CARDIOVASCULAR?
L14            3 S L13 OR L12
L15            3 DUP REM L14 (0 DUPLICATES REMOVED)

     FILE 'CAPLUS' ENTERED AT 08:03:20 ON 24 JAN 2004
L16            0 S L5 AND CARDIOVASCULAR?

     FILE 'USPATFULL' ENTERED AT 08:06:28 ON 24 JAN 2004
L17           63 S L1
L18          332 S VANAD? (10A) (CYCLOPENTADIEN? OR DICYCLOPENTADIEN? OR BISCYCL
L19           41 S VANADOCEN?
L20          359 S L17 OR L18 OR L19
L21            1 S L5 (500A) (ANGIOGEN? OR ANTIANGIOGEN? OR (INHIBIT? (10A) (BLO
L22            0 S L5 (500A) (VASCULAR? OR CARDIOVASCULAR? OR DIABET?)

=> d que l6; d que l15; d que l22
L1          2496 SEA FILE=REGISTRY VANAD? AND (CYCLOPENTADIEN? OR DICYCLOPENTADI
                 EN? OR BISCYCLOPENTADIEN?)
L2          1309 SEA FILE=CAPLUS L1
L3           811 SEA FILE=CAPLUS VANAD? (10A) (CYCLOPENTADIEN? OR DICYCLOPENTADI
                 EN? OR BISCYCLOPENTADIEN? OR ?CYCLOPENTADIENYL)
L4          1512 SEA FILE=CAPLUS L2 OR L3
L5          1551 SEA FILE=CAPLUS L4 OR VANADOCEN?
L6             1 SEA FILE=CAPLUS L5 (200A) (ANGIOGEN? OR ANTIANGIOGEN? OR
                 (INHIBIT? (10A) (BLOOD)) OR ((INHIBIT? OR PREVENT? OR PROPHYLA?
                  OR CONTROL? OR TREAT?) (10A) RESTENOSIS) OR HYPERPLAS? OR
                 ARTHROPATH? OR PROLIFERATIVE DISORDER# OR NEOVASCULAR? OR
                 RETINOPATH? OR HEMANGIOM? OR ARTERY OR ARTERIES OR RETINA#)


L8           109 SEA VANAD? (20A) (CYCLOPENTADIEN? OR DICYCLOPENTADIEN? OR
                 BISCYCLOPENTADIEN? OR ?CYCLOPENTADIENYL)
L9           189 SEA L8 OR VANADOCEN?
L10            1 SEA L9 (200A) (ANGIOGEN? OR ANTIANGIOGEN? OR (INHIBIT? (10A)
                 (BLOOD)) OR ((INHIBIT? OR PREVENT? OR PROPHYLA? OR CONTROL? OR
                 TREAT?) (10A) RESTENOSIS) OR HYPERPLAS? OR ARTHROPATH? OR
                 PROLIFERATIVE DISORDER# OR NEOVASCULAR? OR RETINOPATH? OR
                 HEMANGIOM? OR ARTERY OR ARTERIES OR RETINA#)
L11            1 SEA L9 (200A) (VASCULAR? OR DIABET?)
L12            2 SEA L10 OR L11
L13            1 SEA L9 AND CARDIOVASCULAR?
L14            3 SEA L13 OR L12
L15            3 DUP REM L14 (0 DUPLICATES REMOVED)
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L1          2496 SEA FILE=REGISTRY VANAD? AND (CYCLOPENTADIEN? OR DICYCLOPENTADI
                 EN? OR BISCYCLOPENTADIEN?)
L2          1309 SEA FILE=CAPLUS L1
L3           811 SEA FILE=CAPLUS VANAD? (10A) (CYCLOPENTADIEN? OR DICYCLOPENTADI
                 EN? OR BISCYCLOPENTADIEN? OR ?CYCLOPENTADIENYL)
L4          1512 SEA FILE=CAPLUS L2 OR L3
L5          1551 SEA FILE=CAPLUS L4 OR VANADOCEN?
L22            0 SEA FILE=USPATFULL L5 (500A) (VASCULAR? OR CARDIOVASCULAR? OR
                 DIABET?)
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=> d l6 bib ab kwic

Date no good

L6 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:275687 CAPLUS
DN 135:220738
TI X-ray structure, solution properties, and biological activity profile of **vanadocene**(IV) acetylacetonate complex, [VCp2(acac)](CF3SO3): a dual-function anti-cancer agent with anti-**angiogenic** and anti-mitotic properties
AU Ghosh, P.; Ghosh, S.; Navara, C.; Narla, R. K.; Benyumov, A.; Uckun, F. M.
CS Department of Chemistry, Parker Hughes Institute, Parker Hughes Cancer Center, St. Paul, MN, 55113, USA
SO Journal of Inorganic Biochemistry (2001), 84(3-4), 241-253
CODEN: JIBIDJ; ISSN: 0162-0134
PB Elsevier Science Inc.
DT Journal
LA English
AB The structure of [V(.eta.5-C5H5)2(CH3C(O)CHC(O)CH3)](O3SCF3) (1) (=[VCp2(acac)](O3SCF3)), a dual-function anti-cancer agent with anti-angiogenic and anti-mitotic properties, was detd. by single-crystal X-ray diffraction. The geometry is well described as a pseudo-tetrahedral like structure with the centroids of the cyclopentadienyl rings and the two oxygen atoms of the acetylacetonate ring in the ancillary positions of the central vanadium (IV) atom. The bisector of the V(acac) fragment deviates from the C2 axis of the ligand framework by only 4.degree., compared to a deviation of 7.degree. for the V(acac) fragment in the tetramethylethano-bridged vanadocene acetyl acetonate complex. Crystal data for 1: space group, P21/c; a=7.5544(9) A, b=14.936(2) A, c=16.193(2) A, .beta.=102.901(2).degree., V=1781.0(4) A3; Z=4; R=0.0506 for 2310 reflections with I>2.sigma.(I). This report also details the ESR, UV/Vis spectroscopy, electrochem. properties and the biol. activity profile of this potent anti-cancer agent.
RE.CNT 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
TI X-ray structure, solution properties, and biological activity profile of **vanadocene**(IV) acetylacetonate complex, [VCp2(acac)](CF3SO3): a dual-function anti-cancer agent with anti-**angiogenic** and anti-mitotic properties
IT **Angiogenesis** inhibitors
Antitumor agents
Crystal structure
Cyclic voltammetry
ESR (electron spin resonance)
Stability
UV and visible spectra
(properties and biol. activity of antitumor **vanadocene**(IV) acetylacetonate complex)

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=> d his l8-

     (FILE 'MEDLINE, WPIDS, CANCERLIT, DRUGU, IMSDRUGCONF, JAPIO, MEDICONF,
     PHARMAML, PHIC, PHIN' ENTERED AT 07:58:09 ON 24 JAN 2004)
L8          109 S VANAD? (20A) (CYCLOPENTADIEN? OR DICYCLOPENTADIEN? OR BISCYCL
L9          189 S L8 OR VANADOCEN?
L10           1 S L9 (200A) (ANGIOGEN? OR ANTIANGIOGEN? OR (INHIBIT? (10A) (BL
L11           1 S L9 (200A) (VASCULAR? OR DIABET?)
L12           2 S L10 OR L11
L13           1 S L9 AND CARDIOVASCULAR?
L14           3 S L13 OR L12
L15           3 DUP REM L14 (0 DUPLICATES REMOVED)

=> d que
L8          109 SEA VANAD? (20A) (CYCLOPENTADIEN? OR DICYCLOPENTADIEN? OR
                BISCYCLOPENTADIEN? OR ?CYCLOPENTADIENYL)
L9          189 SEA L8 OR VANADOCEN?
L10           1 SEA L9 (200A) (ANGIOGEN? OR ANTIANGIOGEN? OR (INHIBIT? (10A)
                (BLOOD)) OR ((INHIBIT? OR PREVENT? OR PROPHYLA? OR CONTROL? OR
                TREAT?) (10A) RESTENOSIS) OR HYPERPLAS? OR ARTHROPATH? OR
                PROLIFERATIVE DISORDER# OR NEOVASCULAR? OR RETINOPATH? OR
                HEMANGIOM? OR ARTERY OR ARTERIES OR RETINA#)
L11           1 SEA L9 (200A) (VASCULAR? OR DIABET?)
L12           2 SEA L10 OR L11
L13           1 SEA L9 AND CARDIOVASCULAR?
L14           3 SEA L13 OR L12
L15           3 DUP REM L14 (0 DUPLICATES REMOVED)

=> d 1-3 bib hit
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Date no good

L15 ANSWER 1 OF 3 CANCERLIT on STN
AN 2002081591 CANCERLIT
DN 21267822 PubMed ID: 11374587
TI X-ray structure, solution properties, and biological activity profile of vanadocene(IV) acetylacetonate complex,.
AU Ghosh P; Ghosh S; Navara C; Narla R K; Benyumov A; Uckun F M
CS Parker Hughes Cancer Center, Department of Chemistry, Parker Hughes Institute, St. Paul, MN 55113, USA.
SO JOURNAL OF INORGANIC BIOCHEMISTRY, (2001 Apr) 84 (3-4) 241-53.
Journal code: 7905788. ISSN: 0162-0134.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS MEDLINE; Priority Journals
OS MEDLINE 2002010691
EM 200112
ED Entered STN: 20020726
Last Updated on STN: 20020726
AB The structure of [V(eta5-C5H5)2(CH3C(O)CHC(O)CH3)](O3SCF3) (1) (=[VCp2(acac)](O3SCF3)), a dual-function anti-cancer agent with anti-**angiogenic** and anti-mitotic properties, was determined by single-crystal X-ray diffraction. The geometry is well described as a pseudo-tetrahedral like structure with the centroids of the **cyclopentadienyl** rings and the two oxygen atoms of the acetylacetonate ring in the ancillary positions of the central **vanadium** (IV) atom. The bisector of the V(acac) fragment deviates from the C2 axis of the ligand framework by only 4 degrees, compared to a deviation of 7 degrees for the V(acac) fragment in the tetramethylethano-bridged **vanadocene** acetyl acetonate complex. Crystal data for 1: space group, P2(1)/c; a=7.5544(9) A, b=14.936(2) A, c=16.193(2) A, beta=102.901(2) degrees, V= 1781.0(4) A3; Z=4; R=0.0506 for 2310 reflections with I> 2sigma(I). This report also details the electron paramagnetic resonance, UV/Vis spectroscopy, electrochemical properties

and the biological activity profile of this potent anti-cancer agent.

L15 ANSWER 2 OF 3 DRUGU COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2001-25427 DRUGU S
TI Intravaginal toxicity studies of a gel-microemulsion formulation of spermicidal vanadocenes in rabbits.
AU D'Cruz O J; Uckun F M
CS Parker-Hughes-Inst.
LO St. Paul, Minn., USA
SO Toxicol.Appl.Pharmacol. (170, No. 2, 104-12, 2001) 3 Fig. 4 Tab. 34 Ref.
CODEN: TXAPA9 ISSN: 0041-008X
AV Department of Reproductive Biology, Parker Hughes Institute, St. Paul, Minnesota 55113, U.S.A.
LA English
DT Journal
FA AB; LA; CT
FS Literature
AB Intravaginal **vanadocene** acetylacetonato monotriflate (VDACAC) or **vanadocene** dithiocarbamate (VDDTC) via a gel-microemulsion in rabbits did not cause epithelial ulceration, edema, leukocyte influx or **vascular** congestion. Only minimal to moderate irritation was observed. Decreased epithelial and stromal proliferating cell nuclear antigen (PCNA) expression occurred in tissues exposed to the high dose of VDACAC or VDACAC and VDDTC. Neither VDACAC nor VDDTC induced apoptosis in vaginal tissues. Clinical chemistry profiles were unchanged. Vanadium was not incorporated into rabbit tissues and body fluids above 1 ug/g. Results suggest that **vanadocenes** have potential as a new class of non-detergent-type vaginal contraceptive agents.

Date no good

L15 ANSWER 3 OF 3 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2000-431026 [37] WPIDS
DNN N2000-321692 DNC C2000-130905
TI Electrode system, especially for amperometric oxygen sensors for medicinal diagnostic use, having elemental carbon-based counter-electrode to provide long working life.
DC A96 B04 S03
IN OFFENBACHER, H
PA (HOFF) HOFFMANN LA ROCHE & CO AG F; (AVLV) AVL MEDICAL INSTR AG
CYC 21
PI WO 2000031524 A2 20000602 (200037)* DE 20p
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: JP US
EP 1141691 A2 20011010 (200167) DE
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
US 2002005352 A1 20020117 (200212)
AT 9801930 A 20020315 (200223)
AT 409798 B 20020915 (200269)
JP 2002530672 W 20020917 (200276) 26p
ADT WO 2000031524 A2 WO 1999-AT279 19991118; EP 1141691 A2 EP 1999-972736 19991118, WO 1999-AT279 19991118; US 2002005352 A1 Cont of WO 1999-AT279 19991118, US 2001-860073 20010517; AT 9801930 A AT 1998-1930 19981119; AT 409798 B AT 1998-1930 19981119; JP 2002530672 W WO 1999-AT279 19991118, JP 2000-584288 19991118
FDT EP 1141691 A2 Based on WO 2000031524; AT 409798 B Previous Publ. AT 9801930; JP 2002530672 W Based on WO 2000031524
PRAI AT 1998-1930 19981119
AB WO 200031524 A UPAB: 20000807
NOVELTY - An electrode system including a working electrode, a counter-electrode and an electrolyte, where the counter-electrode is formed from a material containing elemental carbon, is new.
USE - The electrode systems are specifically used for electrochemical sensors, especially amperometric oxygen sensors, particularly miniaturized amperometric oxygen sensors (all claimed). Such electrodes, e.g. Clark

electrodes, are useful for measuring the partial pressure of oxygen in blood to monitor the status of the **cardiovascular** system and metabolic processes (i.e. in medicinal diagnostic applications).

ADVANTAGE - The systems have better long-term stability and longer working life than conventional systems. Working electrodes are not subject to deposition (which could reduce the polarizability of the working electrodes and cause undesirable side-effects. Typically a Clark oxygen electrode having carbon electrodes gives a constant current density for ca. 6 months, whereas the current density using a noble metal (e.g. silver) electrode is halved within 3-4 months or less.

Dwg.0/4

TECH UPTX: 20000807

TECHNOLOGY FOCUS - INSTRUMENTATION AND TESTING - Preferred System: The counter-electrode is anodically connected, and is formed from a mixture of carbon (preferably graphite, carbon black, carbon fiber and/or vitreous carbon) and a polymer. The material of the counter-electrode consists of a (possibly screen-printable) paste or an injection-moldable mixture containing carbon and a thermoplastic polymer or a crosslinkable thermosetting polymer. The counter-electrolyte and/or the electrolyte contains at least one mediator, preferably a complex of , a transition metal oxide, specifically at 1-30% in the electrode material of the counter-electrode or at a concentration of at most 3 mM in the electrolyte. In particular the counter-electrode is a mixture of carbon and nitrilo-butyl rubber and the electrolyte contains dimethyl ferrocenedicarboxylate as mediator; or the counter-electrode is a mixture of graphite and vinyl resin and the electrolyte contains dimethyl ferrocenedicarboxylate or manganese dioxide as mediator. The electrolyte contains ethylene glycol and/or water as solvent, plus sodium chloride as conductivity salt and/or phosphate buffer.

TECHNOLOGY FOCUS - POLYMERS - Preferred Materials: The counter-electrode contains a polymer selected from vinyl resins, polyolefins, silicones and elastomers based on polyurethanes, polybutadiene or butadiene copolymers, especially nitrilo-butyl rubber. The polymer may contain additives, especially plasticizers, extrusion auxiliaries and stabilizers.

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Mediators: The mediator is a complex of a transition metal (specifically manganese, iron, cobalt or **vanadium**), preferably:

(i) a complex of a **cyclopentadienide** anion, especially ferrocene or a derivative, particularly dimethyl ferrocenedicarboxylate, its hydrolysis product or a salt of ferrocene;

(ii) a manganese (II), cobalt (II) or vanadium (IV) phthalocyanine complex; or

(iii) a manganese (III) or cobalt (II) complex of 2,3,7,8,12,12,17,18-octaethyl-21H,23H-porphin.

Alternatively the mediator is tetrathiafulvalene, 7,7,8,8-tetracyano-quinodimethane or a derivative or complex, especially a 1 : 1 complex of tetrathiafulvalene and 7,7,8,8-tetracyano-quinodimethane.

TECHNOLOGY FOCUS - INORGANIC CHEMISTRY - Preferred Compounds: The mediators also include transition metal oxides, preferably of medium valency, especially manganese dioxide; and iron hexacyanoferrate.

Different ✓ inventive entity

L21 ANSWER 1 OF 1 USPATFULL on STN
AN 2003:291180 USPATFULL
TI Vanadium compounds as anti-proliferative agents
IN Uckun, Faith M, White Bear Lake, MN, United States
Navara, Christopher S, Plymouth, MN, United States
PA Parker Hughes Institute, Roseville, MN, United States (U.S. corporation)
PI US 6642221 B1 20031104
AI US 2000-713544 20001115 (9)
DT Utility
FS GRANTED
EXNAM Primary Examiner: Pak, John
LREP Merchant & Gould P.C.
CLMN Number of Claims: 7
ECL Exemplary Claim: 1
DRWN 0 Drawing Figure(s); 0 Drawing Page(s)
LN.CNT 1000
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

One day earlier than this case

AB Vanadium compounds as anti-proliferative agents. These compounds act to disrupt mitotic and meiotic spindle formation and thus are useful to prevent cell mitosis (proliferation) and meiosis.

CLM What is claimed is:

1. A method for inhibiting mitosis or meiosis in a non-cancer cell comprising administering to the non-cancer cell an effective mitosis or meiosis inhibiting amount of a vanadium compound having the following structure: ##STR4## wherein, R.sub.1 and R.sub.2 are each independently a monodentate ligand or together form a bidentate ligand; R.sub.3 and R.sub.4 are each independently a monodentate ligand or together form a bidentate ligand; and R.sub.5 is a monodentate ligand, or is absent; wherein at least one of R.sub.1 and R.sub.2 or R.sub.3 and R.sub.4 combine together to form a bidendate ligand selected from the group consisting of acac, Bpy, Hfacac, Cat, Dtc, PH, acetohydroxamic acid, Phen, or a derivative thereof.

✓ 2. The method of claim 1, wherein each monodentate ligand is selected from the group consisting of halo, OH.sub.2, O.sub.3SCF.sub.3, N.sub.3, CN, OCN, SCN, SeCN, and a cyclopentadienyl ring, wherein the cyclopentadienyl ring is optionally substituted with one or more (C.sub.1-C.sub.3)alkyl, and each bidentate ligand is selected from the group consisting of acac, Bpy, Hfacac, Cat, Dtc, PH, acetohydroxamic acid, Phen, or a derivative thereof.

3. The method of claim 2, wherein each bidentate ligand is optionally substituted with one or more of halo, (C.sub.1-C.sub.3) alkyl, (C.sub.1-C.sub.3) alkoxy, halo (C.sub.1-C.sub.3) alkyl, or a derivative thereof.

4. The method of claim 1, wherein R.sub.1 and R.sub.2 together form a bidentate ligand selected from the group consisting of acac, Bpy, Hfacac, Cat, Dtc, PH, acetohydroxamic acid and derivatives thereof.

5. The method of claim 4, wherein the bidentate ligand is acac or a derivative thereof.

6. The method of claim 1, wherein said vanadium compound is: VCp.sub.2(acac), VCp.sub.2(hfacac), VCp.sub.2(bpy), VCp.sub.2(cat), VCp.sub.2(dtc), VCp.sub.2PH, or VCp.sub.2H wherein H represents acetohydroxamic acid bidendate ligand.

7. A method for treating a non-cancer proliferative disorder in a subject, comprising administering to the subject an effective mitosis inhibiting amount of a vanadium compound of structure II: ##STR5## wherein, R.sub.1 and R.sub.2 are each independently a monodendate ligand or together form a bidendate ligand; R.sub.3 and R.sub.4 are each independently a monodendate ligand or together form a bidendate ligand;

and R.sub.5 is a monodendate ligand, or is absent; wherein (i) at least one of R.sub.1 and R.sub.2 or R.sub.3 and R.sub.4 combine together to form a bidendate ligand selected from the group consisting of acac, Bpy, Hfacac, Cat, Dtc, PH, acetohydroxamic acid, Phen, or a derivative thereof, and (ii) at least one of R.sub.1, R.sub.2, R.sub.3, R.sub.4 or R.sub.5 is a cyclopentadienyl ring.

L21 ANSWER 1 OF 1 USPATFULL on STN
2003:291180 Vanadium compounds as anti-proliferative agents.
Uckun, Faith M, White Bear Lake, MN, United States
Navara, Christopher S, Plymouth, MN, United States
Parker Hughes Institute, Roseville, MN, United States (U.S. corporation)
US 6642221 B1 20031104
APPLICATION: US 2000-713544 20001115 (9)
DOCUMENT TYPE: Utility; GRANTED.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM The present invention is drawn to the use of **vanadium** compounds, preferably **vanadium cyclopentadienyl** compounds (**vanadocenes**) and oxovanadium compounds, including, but not limited to those described in published PCT applications WO99/36063; WO 00/27389; and WO 00/35930. Vanadium compounds useful in the method invention include **vanadocene** compounds such as **vanadocene** dichloride (VDC), vandocene acetylacetonate (VDacac), and those vanadium compounds shown below. Specifically, the present invention relates to the finding that. . . and meiosis. The anti-mitotic and anti-meiotic activity makes these compounds particularly attractive anti-proliferative agents, particularly for the treatment of non-cancer **proliferative disorders**.